REVIEW OF LITERATURE
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Burn is one of the oldest form of injury and a universal problem. Even the prehistoric man suffered from burns from lighting, molten lava and steam of hot springs. The Epidemiology of burns has gradually changed with time, reflecting the changing environment of man. Electrical, chemical and radiation burns have been the price for industrialization. In addition homicidal and suicidal burns have increased as a result of social development. Over the years there has been progressive refinement in the treatment of burns. All research is being aimed at promoting tissue healing and reducing the chances of septicaemia. It is very important to know how this outlook towards treatment of burns has changed over the centuries.

Ancient methods
Ancient methods of treatment in ancient era was mainly local application which was highly different and often exotic. In the 5th and the 6th century BC, Egyptians treated burn by mixture of gum, goat’s hair and milk of a lady who had given birth to a son. Chinese and Japanese were using tincture and extracts from tealeaves in around 480 BC. Romans
had tried other innovative methods like honey and bran, vinegar and wine. The mixture of resin and bitumen was used by Hippocrates. He also used warm vinegar soaked dressing to relieve pain. In ancient Rome, Ceicus suggested a mixture of honey and bran for local application. Gallar suggested local application of vinegar and wine on burn surface. In the 9th century AD Paulus of Aegina used various emollient preparations. A mixture of white lead, oil of roses and wax had been used by Rhozer (580-920 AD). Ice cold water was used on burn surface by Arabian physicians. Amrose Pare (1517-1590) suggested the use of ointment in treatment of burn. Clowes (1591) used 5 different complex preparations in the treatment of burn. Vinegar and chalk was used locally by David Clegron (1792). Pressure dressing as a mode of treatment was suggested by Edward Kentish (1797) to relieve pain and to stop blister formation. Ice cold water acts as a good analgesic and prevents oedema formation was suggested by Sir. James Earle (1799) and used in the treatment of burns.

**The later to present day:**—Between 1833 to 1868 the dry method of dressing remained supreme. This form of therapy almost replaced the purposeless use of carosine oil and Linementon aquae Calcis (Syme 1834 in his principles of surgery).
But in 1871 Copland suggested exposure method was best method of the treatment of burn.

The discovery of antiseptic properties of carbolic acid by Joseph Lister heralded its use in the treatment of burns in 1898. Carbolic acid oil (2.5%), was applied to injury area and dressing removed every day. The disadvantage was local gangrene converting the partial thickness burn into full thickness burn. The local absorption of carbolic acid caused adverse effects like nausea, vomiting, muscle twitching, excitement, weakness, hypotension and perspiration.

The period following carbolic acid era, was an important period called saline wet dressing antiseptic era extending between 1885 to 1910 for treatment of burns. Since then the various topical agents and treatment methods have been used in burn sepsis which include wet dressing with sodium bicarbonate followed by application of solution of picric acid or boric acid as advocated by Oppenheimer (1906). Picric acid absorption from local injury site may cause tachycardia, nausea, vomiting, diarrhea, fever, renal failure and coma, was recognized by A. Maclevenen (1903) and E.J. Elliot (1906). On other hand boric acid may cause
rashes with desquamation of skin, restlessness, confusion, weakness, hypothermia, hypotension, tachycardia and renal failure.

Wet dressing gave way to wax as a modality of treatment. Wax containing 250 mg % Betanaphthol was applied at a temperature of 50 to 600 C. This was recommended topically between 1910 to 1926. The adverse effects were extensive with renal and hepatic damage and convulsion and even death.

Local application of tannic acid on burn surface was started by Edward Clark and Devitson in 1925 at Henry Ford hospital. Later on in 1944 Maclux in the same hospital described it as a hepatotoxic agent and attributed many deaths due to its toxicity. Gentian violet as an escharolytic agent in burn surface was tried by (Aldriage, 1933). Allen and Koch (1942) suggested the use of Petroleum gauze locally with strict immobilisation as further advancement in the management of burn injury in IIInd world war "Exposure Method" of treatment of burn wound must have actually been used for several centuries. The credit for reintroduction of exposure method as modality for treatment of burn goes to Wallace (1949) of Edinburgh and Pualki, Artzi and Blocker (1950) of
U.S.A. Later on other surgeons accepted the same method with a view that formation of crust acts as a physiological covering of burn wound, thus reducing the disadvantages of raw area. Exposure causes drying of the wound and inhibition of bacterial proliferation, besides, ultraviolet light also acts as a deterrent to bacterial growth. The use of topical agent further enhances the control of bacterial growth already achieved.

Inspite of various treatment modalities advocated during the last century, none of them could significantly reduce the incidence of burn morbidity and mortality.

The simultaneous progress in other fields like improvement in microbiological techniques, culture media etc. aided in identifying the organism responsible for death. The principal cause of death was septicaemia and organism responsible was staphylococci (Ludbug Reise and Artz 1953). The world war had heralded a new era in the treatment of infection with the development of antibiotics like penicillin and other associated compounds in controlling most of the gram positive and gram negative bacteria.
Because of systemic delivery of antibiotics at the burn wound sites is sub-optimal, topical agent should play an important role in the management of burn injury. A number of techniques with topical agents have been evolved in mid 1960, that have substantially decreased the incidence of burn bound sepsis. Each has its own advantage and disadvantages.

**BIODRESSING**

The main cause of morbidity and mortality in burn patients is toxiaemia due to absorption of toxins from injured surface of burn invaded by micro-organism, so the epoch making discovery in the treatment of burns was the advent of 'Biological dressing' for restoration of impaired barrier. If an ideal skin substitute could be discovered, it could bring about a drastic change in the outlook to the treatment of burns. Eschar could be excised in early in post-burn period and then covered with skin substitute. In about a week or two the patients could be discharged. Autologous healthy skin grown in tissue culture can be used to replace this.

In brief an ideal skin substitute should possess the following properties -
1. Should adhere rapidly and strongly with the underlying raw areas.
2. Should have water vapour characteristics like that of normal skin.
3. Should be elastic enough to stretch freely over joints.
4. Should be durable.
5. An intact bacterial barrier.
6. Should not be antigenic.
7. Should be easy to apply and remove.
8. Should be cheap.
9. Should be homeostatic.

The various materials that could be used as a skin substitutes are -

I. **BIOLOGIC:**
   
   (a) **Human allograft (Homograft):**
       - Living donor
       - Cadaver donor fresh
       - Cadaver donor frozen
       - Amniotic membrane

   (b) **Xenograft (Heterograft)**
       - Living donor fresh, Frozen radiated or dried.
(c) Tissue derivatives:
- Collagen sheet fabric or sponges
- Bioplast fibrin.

II. SYNTHETIC:
- Solid silicon polymer membrane
- Other plastics
- Microporous materials

III. COMPOSITE MATERIALS:
- Surface membrane:-(Silicon, microporous, trydron).
- Adherent substrate: - Collagen, cotton gauze, synthetic polymer, sponge, Vetour, flecking or fabric.

LIMITATION OF BIOLOGICAL DRESSING:
Inspite of being the best dressing material for burn wound, they have certain disadvantage in form of -
1. Paucity in availability of autograft & other dressings.
2. Overwhelming financial overtones (which turn out to be an important consideration in a poor country like India).
3. Subgraft suppuration.
5. Lyophilised allograft skin shows fewer adherence to the wound and is of sufficient thickness, undergoes dermal separation and causes desiccation of exposed dermis.

**Problem of Burn Wound Infections and Topical Agents**

The management of burn wound sepsis is still a very challenging problem in terms of morbidity and mortality. It is the major factor causing death, during the phase of illness. Because the systemic delivery of antibiotics at the burn wound site is sub-optimal, topical agent should play an important role in the management of burn wound sepsis. There are a number of topical agents used in burn sepsis. Yet the search for ideal topical therapy has as yet proved elusive. Over the years the endeavours aimed at topical therapy have been topical oint (Fox CL Jr, Rappole B.W and Stainford W 1969), early escharotomy or skin grafting (Burke JF, Bondoc CC and Quinby WC 1974) or amniotic membrane application (Bose B 1979).

The properties of ideal topical applicable drug, given by Zellner P.R and Buggi S. in 1985, is as follows -
(1) The topical agent should have antiseptic properties and wide spectrum of action.
(2) Minimal development of resistance against drug.
(3) Must penetrate the eschar.
(4) Must not harm the viable tissue.
(5) Should not hinder the growth of proliferating tissue.
(6) Must be nontoxic and must not interfere with metabolism.
(7) Must not be antigenic.
(8) Should be cheap.
(9) Must have tanning effect.
(10) Should be easy to administer and to remove.

To assess the effectiveness of topical agents following parameters are used:

1.) Surface culture and sensitivity reflect bacterial infection on the surface of burn wound.
2.) Quantitative estimation of bacterial counts indicating the degree of infection.
3.) Culture of burn wound biopsy provides three parameters for assessment of infection.
   A.) Quantitative bacteriology.
   B.) Qualitative bacteriology.
C.) Histology:–They provide perivascular, perilymphatic and intraluminal accumulation of bacteria prove without doubt invasive bacterial infection (Krupp S, Baechler M, Bille J 19850).

In order to fulfil the above criteria, a number of newer techniques of burn dressings have been evolved. Each has its own advantage and disadvantages. A few important agents, some of which are still in vogue like Mefamide or Sulfamylon (Moncrief 1974), cerium nitrate (Williams W Monafo 1975), 0.5% silver nitrate (Mayer 1960), silver sulphadiazine (Fox CL Jr 1975) and Mercurochrome. These topical agents have more of palliative effect and help only in reducing the local bacterial concentration (from $10^7$ to $10^4$ microbes per gm.), not eradicating the bacteria from the wound (Artz C.P 1979). These agents have deleterious side effects, and can even prove lethal, if the patient is not carefully monitored, for example silver nitrate causes necrobiosis, discolouration of local area due to precipitation of silver ion, serum Na$^+$, K$^+$, and Cl$^-$ deficits and alkalosis (Kulick al 1980). Hence the monitoring the Na$^+$, K$^+$, Cl$^-$ becomes a must. Sulfamylon, although readily diffuses through the eschar, is
potent inhibitor of carbonic anhydrase and it may induce acid base derangement leading to acidosis. With Mercurochrome, toxic amounts of mercury can be absorbed (Steen 1983).

Due to side effects of silver nitrate, another topical anti-microbial Silver Sulphadiazine (S.S.D) was introduced. S.S.D exerts an anti-bacterial action mainly against Pseudomonas, poorly penetrates the eschar, the eschar does not adhere to the dressing and the silver ions are released slowly in a concentration such that they are selectively toxic to pathogens (Rosenksaz 1972). Silver ions act on bacterial cell surface causing alteration in cell wall and cell membrane leading to death. The disadvantages are crystalluria, resistance to sulphonamides and high cost and adverse reactions like burning, rashes, itching and difficulty in daily application on burn surface. But overall SSD is distinctly superior to silver nitrate.

Povidone-Iodine (PVP) has been in use for over a period of four decades. (Garner et al in 1959, Georgide in 1962, Connell in 1964, Copeland in 1972). Nicholas G. Goergide in 1972 found PVP to be one of the best antiseptic agents because of its broad spectrum, good penetrability through the eschar while exerting its microbicidal effect. It
does not harm the surviving and proliferating tissue and has neither antigenicity nor any skin reaction and infecting microorganisms do not develop resistance to it. It also has tanning effect and enhances wound healing by preventing infection.

Povidone-Iodine can easily be applied locally or along with Aserbine (Knock, D.M 1985). P.V.P is effective against a wide range of gram positive and gram negative organism as well as some fungi, spores and viruses (Schwarts, Shires and Spencer, 1988). Prolonged treatment with povidone-Iodine does not have any effect on thyroid gland. But in 1974 Law EJ and McMillan reported adverse effect of PVP on thyroid gland in two patients out of seventy patients.

In 1985 Balogh D, Bauer M and Riccabona G reported that patients treated with PVP may show increased serum iodine level but simultaneous measurement of thyroid hormones failed to reveal any significant impairment of thyroid function apart from depressed T₃ coupled with increased reverse T₃. They also reported that if renal function is unimpaired, the absorbed iodine is quickly excreted and no clinical sign of iodine toxication were observed. In 1991, Nakano S, Uchiyam A of Japan reported that prolonged exposure
to wet PVP can cause chemical burn but no other author observed such type of reaction in their study.

Iodine released from Idophore (Polyvinyl Pyrrolidone) after application of PVP, precipitates the proteins of bacteria and other micro organisms and reacts with exudates to precipitate proteins on wound surface forming a firm crust under which no micro organism can survive.

The efficacy of PVP increases when used with Neosporin powder. Neosporin powder (Wellcome & Burrough’s) contains three ingredients:-

1.) Neomycin sulphate.
2.) Zinc Bacitracin.
3.) Polymyxin-B.

Neomycin is predominantly a locally acting bacteriocidal drug, having adverse effects like otonephrotoxicity and depression of respiratory system. Bacitracin is effective against gram-positive cocci and bacilli and Polymyxin-B is antibacterial against mainly H. pertusis, Pseudomonas, E.coli and other gram negative bacilli and has side effect like acute renal failure and nystagmus. Its systematic absorption is little and allergic reactions are rare.
Because PVP + N was applied as a "crust", because the crusting effect ensures that the locally applied drugs remain at the burn site for a prolonged period and at the same time because subsequent application are applied over the previous one, the patients does not feel any pain after the first application. Even the first application entails only minimal pain. In our opinion, if burn patients can be given an option of pain free local burn own management it would be of immense psychological relief to the patient. In addition, nursing personnel time is reduced by about 70 to 80% on average and therefore treatment cost is less.

In qualitative bacteriology immediate gram staining shows the presence of bacteria and identification of bacteria from wound biopsies provides precise identification. The organism which have been recovered from culture of wound swab and wound biopsies are as follows:-

A.) Gram negative bacilli - Enterobactor spp., Klebsiella, E-coli, pseudomonas aeruginosa etc.

B.) Gram positive bacilli - Enterococci, staph, epidermis, staph. aureus, streptococcus.
C.) Other opportunistic infections – Fungal eg. Candida spp., yeast and viral infection.

The combination of drug treatment utilizing the PVP + Neosporin powder may act as complimentary to each other. Beneficial encouraging results were seen with this combination in term of infection, role & markedly reduce healing time of burn wounds by Sinha R et al in 1988. Following study using multiple subescharal injection of PVP was done.

The subescharal technique is based on original observation of Drs & Moncrief demonstrating the ischemia within a burn wound and the failure of nutrients or systemic and local treatment to reach the subescharal plane. The systemically administered antibiotics can only reach the ischemic area by gradient diffusion from the wound periphery.

Baxter et al 1973 first used subescharal injections of antibiotics in deep burn. Subescharalclysis offers the theoretical advantage of direct administration of antimicrobial to deep burn area where systemic antimicrobials fail to reach. Subescharal injections of PVP helps to decrease the ultimate bacterial concentration in the subescharal plane and help in early escharoclysis, decreasing the bleeding on
separation of eschar and ultimately in preventing septicaemia and death.

In the present study our aim is to assess the efficacy of subescharal injection of P.V.P with surface P.V.P + Neosporin powder, application in term of

- Subescharal bacterial concentration,
- Escharolysis time.

At the same time to see the effect of P.V.P on thyroid function/renal function.